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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/833,799	04/13/2001	Enno Christophers	3774-4	1948

23117 7590 04/09/2003

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EXAMINER
DUFFY, PATRICIA ANN

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 04/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/833,799	Christopher et al
Examiner	**Art Unit**
Patricia A. Duffy	1645

FILE COPY

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jan 29, 2003*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above, claim(s) *1-7, 14, 19, and 20* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *8-13, 15-18, and 21-25* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims *1-25* are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *13*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The response and amendment filed 1-29-03 has been entered into the record.

Claims 1-25 are pending.

Priority

2. If applicant desires priority under 35 U.S.C. 120 based upon a previously filed copending application, specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No._____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

3. Applicant is reminded that in order for a patent issuing on the instant application to obtain the benefit of priority based on priority papers filed in parent Application No. 07/926,371 under 35 U.S.C. 119(a)-(d) or (f), a claim for such foreign priority must be made in this application. In making such claim, applicant may simply identify the application containing the priority papers.

Information Disclosure Statement

4. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not

be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Specification

5. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Election/Restriction

6. Applicant's election of Group II, claims 8-13, 15-18 and 21-25 in Paper No. 11 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

7. Claims 1-7, 14, 19, and 20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 11.

Claim Rejections - 35 U.S.C. § 101

8. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

9. Claims 8-13, 15-18, 24 and 25 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claimed invention is drawn to a protein product of nature. Products of nature are not patentable because

they do not reflect the "hand of man" in the production of the product or manufacturing process. Diamond v. Chakrabarty, 206 USPQ 193 (1980). Additionally, purity of naturally occurring product does not necessarily impart patentability. Ex parte Siddiqui 156 USPQ 426 (1966). However when purity results in new utility, patentability is considered. Merck Co. V. Chase Chemical Co. 273 F. Supp 68 (1967). See also American Wood v. Fiber Disintergrating Co., 90 US 566 (1974); American Fruit Growers v. Brogdex Co. 283 US 1 (1931); Funk Brothers Seed Co. V. Kalo Innoculant Co. 33 US 127 (1948). Filing of arguments and evidence of a new utility imparted by the increased purity of the claimed invention *and amendment to the claims to recite the essential purity* of the claimed products is suggested to obviate this rejection. For example, "An isolated nucleic acid...". .

Claim Rejections - 35 U.S.C. § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 8-13, 15-18 and 21-25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a written description rejection.*

The claims are drawn to nucleic acids encoding functional equivalents/analogues, fragments, variants that are "substantially similar", hybridizing nucleic acids and compounds capable of being modified in vitro or in vivo to a inhibitory polypeptide. The teachings of the specification are limited to a nucleic acid set forth in Figure 13, encoding a polypeptide consisting of the amino acid sequence disclosed therein that has been demonstrated to inhibit human leukocyte elastase. The specification therefore discloses all the nucleic acids encoding the polypeptide consisting of the amino acid structure set forth in Figure 13, including the specific nucleotides set forth in the specification and the Figures. However, the specification does not provide adequate written description of nucleic acids encoding functional equivalents, inhibiting fragments of Figure 13, variants that are "substantially similar", hybridizing nucleic acids and compounds capable of being modified in vitro or in vivo to a inhibitory polypeptide.

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying

characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

With the exception of nucleic acids encoding the polypeptide inhibitor consisting of the amino acid sequence of Figure 13 or the specific nucleic acids described in the Figure, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides, regardless of the simplicity of the method of isolation, absent further guidance. Since the claimed genus encompasses undisclosed protein variants, variant sequences, and allelic gene variants yet to discovered, the full length polypeptide, the disclosed structural feature (i.e., the nucleic acid of Figure 13, encoding a polypeptide of Figure 13) does not constitute a substantial portion of the claimed genus. Absent a written description disclosing a representative number of nucleic acid sequences from this broad class of variants of polynucleotides claimed, the specification fails to show that applicant was "in possession of the claimed invention" at the time the application for patent was filed. The genus of nucleic acids which are allelic variants, analogues, hybridizing and functional fragments is very large, encompassing not only sequences with polymorphisms and mutations compared to the disclosed sequences of Figure 13. Further, no function is required by many of these claimed variants. Thus the genus of nucleic acids encompassed by this claim is extensive, and there does not appear to be any requirement that the nucleic acids share either a particular structure, a particular function, nor a correlation between some partial structure and a particular function. Consequently, the nucleic acid and amino acid of Figure 13 does not appear to constitute a substantial portion of the claimed genus. Since these various variant nucleic acids do not possess defined structure and function, they lack adequate written description, as do vectors and host cells and

methods of making. It is noted that cDNA of Figure 16 is a fragment and not a full-length open reading frame, by virtue of the fact that the start codon is not methionine. The specification, therefore does not disclose what the full-length protein or nucleic acid encoding such. The claims reciting "comprising" and "encoding" language read upon complete gene sequences having in common a nucleotide sequence of Figures 13, 14 or 16 from any source. With the exception of these, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides, regardless of the simplicity of the method of isolation, absent further guidance. Since the claimed genus encompasses undisclosed genes, partial genomic sequences, and genes yet to discovered, the disclosed structural feature does not constitute a substantial portion of the claimed genus. Absent a written description disclosing a representative number of nucleic acid sequences from this broad class of polynucleotides, the specification fails to show that applicant was "in possession of the claimed invention" at the time the application for patent was filed. In addition, the claims recite a nucleic acid probe comprising a nucleotide sequence capable of hybridizing to a nucleic acid comprising a sequence as part of the invention. However, there does not appear to be an adequate written description in the specification as-filed of the essential structural feature of the instantly recited nucleic acids, nor a correlation between a particular structure and function. The genus of nucleic acid probes which would hybridize to a nucleic acid is very large, encompassing not only sequences with polymorphisms and mutations compared to the nucleic acids of Figures 13, 14 and 16, but also sequences having no shared sequence with these sequences since the hybridization could occur within the non coding region or outside of the disclosed nucleic acid. Further, no function is required of this hybridizing probe. Thus the genus of nucleic acids encompassed by this claim is extensive, and there does not appear to be any

requirement that the nucleic acid probes share either a particular structure, a particular function, nor a correlation between some partial structure and a particular function. Consequently, the nucleic acids set forth in Figures 13, 14 and 16 again does not appear to constitute a substantial portion of the claimed genus.

The mere statement that a genus of nucleic acids is part of the invention and reference to a potential method for isolating some of these nucleic acids is not adequate written description of those nucleic acids. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993), and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. Consequently, Applicant was not in possession of the instant claimed invention. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision. (See page 1115.) Further, Reagents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398, appears to be directly relevant to the instant fact pattern. In Eli Lilly the specification and generic claims to all cDNAs encoding for vertebrate or mammalian insulin did not describe the claimed genus because they did not set forth any common features possessed by members of the genus that distinguished them from others. Id. at 1568, 43 USPQ2d at 1405. Nor did the specification describe a sufficient number of species within

the very broad genus to indicate that the inventors had made a generic invention, i.e., that they had possession of the breadth of the genus, as opposed to merely one or two such species. Id.

13. Claims 21 and 24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The claims are drawn to any nucleic acid sequence shown in Figure 13 that encodes a polypeptide or fragment that possesses inhibitory activity against human leukocyte elastase. The teaching of specification in regard to Figure 13, teaches a single amino acid sequence that encodes a single polypeptide with inhibitory activity. The claims include any of polypeptide in any reading frame that would encodes such. The specification provides no conception of multiple inhibitory polypeptides or fragments determined by the nucleic acid sequence as set forth in Figure 13. As such, because the claims are directed to any inhibitory polypeptide as it relates to the nucleic acid disclosed in Figure 13, the claims are deemed new matter.

14. Claims 8-13 and 15-18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to complements, hybridizing nucleic acids and probes that do not encode a polypeptide leukocyte elastase inhibitor. The specification fails to provide any teaching on how to use complements, hybridizing nucleic acids and probes in any patentable manner. The use disclosed for nucleic acids in the specification to produce the

polypeptide for therapeutic purposes does not extend to non-coding nucleic acids such as that are complements, hybridizing nucleic acids an probes. For example, "complementary" is routinely used in the art to describe the opposite (reverse complement) strand of a given DNA sequence, therefore the claim reads upon a polypeptide encoded by a sequence antisense to the coding strand of the inhibitory polypeptide, or the antisense. It is well known that antisense sequences do not encode products related to the sense strand, for example, the 5'- 3' directionality is reversed, and therefore each codon triplets is read in the reverse orientation (encoding a different amino acid in most instances) and the N and C terminal of the encoded product is reversed. Applicant has not provided any guidance or working examples which would lead one of skill in the art to predict, firstly, that the antisense strand of the coding strand set forth in Figure 13 does, in fact, encode protein product (e.g. start sequences, methionine codon, a substantial open reading frame, stop and other termination signals). Further, one of skill in the art would not predict such a product would be structurally or functionally related to the elastase inhibitor, and Applicant has not provided any potential means of using such an unrelated product.

15. Claims 8-13. 15-18 and 21-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As to claims 8-13, 15-18 and 21-25, the claims lack precision by not specifically reciting the chemical formulae and merely reference figures with several formulae. Where possible, claims are to be complete in themselves. Incorporation by reference to a specific figure or table "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate

by reference than duplicating a drawing or table into the claim. Incorporation by reference is a necessity doctrine, not for applicant's convenience." Ex parte Fressola, 27 USPQ2d 1608, 1609 (Bd. Pat. App. & Inter. 1993). Applicants are directed to MPEP 2173.05(s) "Reference to Figures or Tables". Since the amino acids and nucleic acids can be represented by conventional chemical formulae, incorporation by reference in the claims is not a necessity. Correction is required.

As to claims 21-25, the claims direct one to the nucleic acid of Figure 13, however, the figure cites 2 nucleic acids and therefore lacks precision as to the metes and bounds of what is being claimed. Additionally, the nucleic acids of the figure have at least 6 reading frames, three forward and three reverse and it is not clear from the claims what reading frame encodes the claimed peptide inhibitor.

The term "substantially" in claim 11 is a relative term which renders the claim indefinite. The term "substantially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim Rejections - 35 U.S.C. § 102 or 103

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

17. Claims 8, 11, and 15 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by New England Biolabs Catalog, 1986/87.

New England Biolabs teaches Eco-RI linkers. The linkers are a fragment of the nucleic acid sequence set forth in Figure 13 corresponding to the coding strand residues 1-5). Further, the linker would hybridize to the sequence of Figure 13, and perform the function as a probe absent convincing factual evidence to the contrary. Further, a fragment is a single nucleic acid sequence and therefore meet the limitation of "fragment" in all circumstances.

18. Claims 12, 13, 17 and 18 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Maniatis et al, Molecular Cloning A Laboratory Manual, Cold Spring Harbor Laboratory, 1982.

Maniatis et al teach vectors for cloning and expression of eukaryotic genes at pages 403-419 in *Escherichia coli* (a host cell). Each of these vectors is "capable of" expressing the gene of interest in the host cell. Further, Maniatis et al teach how to insert genes of interest into the plasmids, insert the plasmids into host cells for production of the protein of interest at pages 247-251. The art meets the claimed

invention because the plasmids, host cells, etc are all "capable of" production of any polypeptide and there is no positive limitation in the claim that provides for the production of any specific protein sequence. Applicants are directed to claim 16 for suitable language to limit the vectors/host cells etc to refer to specific claimed nucleic acid sequences.

19. Claims 7, 8, 9, 11, 12, 13, 15, 16, 17, 18 and 21-25 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Remold-O'Donnell, U.S. Patent 5,370,991, with full priority to Feb 23, 1989.

Remold-O'Donnell teaches the gene encoding a human monocyte elastase inhibitor (see claim 2). Remold-O'Donnell teaches that the nucleic acid is inserted into conventional expression vectors and expressed in suitable host cells under conditions to produce the inhibitor peptide. Remold-O'Donnell teaches the insertion of the cDNA encoding the inhibitor in to a suitable expression system. Remold-O'Donnell contemplates oligonucleotides, sense or antisense or RNA corresponding to the disclosed oligonucleotides (see column 2, line 36, to column 3, line 13). Inasmuch as the claims include, nucleic acid comprising fragments that have inhibitory activity (i.e. the claimed nucleic acid encodes an inhibitory polypeptide that has a single amino acid in common with that of the prior art) and analogues and variants with no structure, the claims are clearly anticipated.

Allowable Subject Matter

Claim A. An isolated nucleic acid consisting of a nucleotide sequence encoding the polypeptide Ala.....Gln (i.e. the specifically recited sequence set forth in Figure 13).

Claim B. The nucleic acid of claim A, wherein in the nucleotides sequence is GCT....CAA(the specific nucleic acid sequence set forth in Figure 13/14/16 coding for the inhibitory polypeptide).

Claim C. An isolated replicable plasmid expression vehicle comprising as the insert, the isolated nucleic acid of claim A.

Claim D. An isolated transformed host cell comprising the expression vehicle of claim C.

Claim E. A process for the preparation of a replicable expression vehicle comprising inserting the nucleic acid of claim A into a vector at an appropriate insertion site so that a replicable plasmid expression vehicle is obtained which is capable of directing the synthesis of a polypeptide encoded by the nucleic acid.

Claim F. A process for producing a polypeptide comprising culturing the host cell of claim D under conditions sufficient to produce the polypeptide.

Claim G. A process for the preparation of a transformant host cell comprising transforming a host cell by the insertion therein of the expression vehicle of claim C.

Status of Claims

20. No claims are allowed.

21. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy, Ph.D. whose telephone number is (703) 305-7555. The examiner can normally be reached on Monday-Friday from 9:30 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308-3909.

Patricia A. Duffy, Ph.D.

April 3, 2003

Patricia A. Duffy, Ph.D.
Primary Examiner
Group 1600